DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 23 February 2009.

Claim Status

Claims 1, 3-5, 7, 8, 10, 12, 13, 16-21 and 24-41 are pending. Claims 2, 6, 9, 11, 14-15, and 22-23 are cancelled. Claims 1, 3-5, 10, 21, 24-30 and 36 are amended. Claims 37-41 are newly added. Claims 1, 3-5, 7, 8, 10, 12, 13, 16-21 and 24-41 are under current examination.

Priority

This application claims benefit as a 371 of PCT/US04/04262 (filed 02/13/2004) which claims benefit of 60/319,946 (filed 02/14/2003) and claims benefit of 60/319,956 (filed 02/19/2003). The instant application has been granted the benefit date, 02/14/2003, from the application 60/319,946.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 13 April 2009 consisting of 7 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

RESPONSE TO ARGUMENTS

35 USC § 102

The rejection of claims 1, 5, 10, 21, 25, 28, 29 and 31 under 35 U.S.C. 102(e) as being anticipated by Yu et al. (US2003/0186916, published 2 Oct 2003) is withdrawn in response to the applicants claim amendments. The applicant's claim amendments have been fully considered and are persuasive. The applicant has amended the claims so that the claimed particles are now "nanoparticles." While the examiner believes this to be an inherent feature of these compositions, Yu et al. does not explicitly indicate the size of their particles. Therefore, the examiner accepts the applicant's argument that this limitation is not taught by Yu et al. Therefore, the examiner hereby withdraws the rejection of claims 1, 5, 10, 21, 25, 28, 29 and 31 under 35 U.S.C. 102(e) as being anticipated by Yu et al.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 7, 8, 10, 12, 13, 16-21, 24-28 and 30-36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002) for the reasons of record and the comments below.

The applicant's arguments have been fully considered but are unpersuasive.

The applicant argues “the cited references, alone or in combination , do not disclose or suggest the claimed invention (Remarks, page 7, parag.4). Contrary to the applicant’s arguments, the cited references suggest the instant claims. Hart is a review article which discusses a variety of nucleic acid formulations including lipopolyplexes (which according to Hart are compositions comprising lipids and cationic polymers that are used as DNA condensing agents) (page 203, section 4). In fact, instant claim 1 is a species of the condensed DNA/lipopolyplexes of Hart, because chitosan is a species of

cationic polymer. Furthermore, both references teach a variety of compositions comprising DNA/ chitosan, and DNA/lipid. Taken together, the Hart and Ni suggest the particular condensed DNA/lipopolyplexes comprising DNA, chitosan and a lipid of the instant claims. Therefore, the examiner finds the applicant's argument unpersuasive.

Further, the applicant has made arguments against each of the references (Hart and Li et al.), indicating that neither provides all the required limitations. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The applicant argues that there is no explicit teaching or suggestion in the references which show a particle comprising a polynucleotide, a lipid, and chitosan is in the nanoscale. The cited art suggest that the particles are in the nanoscale because Hart teaches "nanospheres, in the size range of 200-750nm, can be produced by salt-induced association of cDNA and polycations such as gelatin and chitosan" (page 203, section 3.4).

The applicant argues that "the chitosan-lipid nanoparticles exhibited increased infection efficiency, but they also show a decreased induction of IL-6, a pro-inflammatory cytokine, when compared to chitosan alone" and therefore indicate nonobviousness because of a greater than expected result (Remarks, pages 9-10, emphasis added by applicant). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon

which applicant relies (i.e., decreased induction of IL-6) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, the examiner finds the applicant's argument unpersuasive.

Therefore, the examiner hereby maintains the rejection of claims 1, 3-5, 7, 8, 10, 12, 13, 16-21, 24-28 and 30-36 under 35 U.S.C. 103(a) as being unpatentable over Hart et al. in view of Ni et al.

The examiner reiterates the pending rejection:

Claims 1, 3-5, 7, 8, 10, 12, 13, 16-21, 24-28 and 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002).

Claim 1 is directed to a particle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide. Hart is a review article which discusses a variety of nucleic acid formulations including lipopolyplexes (which according to Hart are compositions comprising lipids and cationic polymers that are used as DNA condensing agents) (page 203, section 4). Both Hart and the instant specification define lipoplexes and polyplexes as different from lipopolyplexes or Chlipids. In fact, instant claim1 is a species of the condensed DNA/lipopolyplexes of Hart, because chitosan is a species of cationic polymer. While Hart does not explicitly teach that chitosan can be used to make the lipopolyplexes, Hart does teach chitosan/DNA nanoparticle compositions (page 203, section 3.4), thereby suggesting chitosan's utility as a DNA condensing

agent. Ni et al. teach a variety of compositions comprising DNA/ chitosan, and DNA/lipid. Furthermore, Ni et al. teach that their compositions can contain other materials. Ni et al. teach, "formulations and methods of administration that can be employed when the compound comprises a nucleic acid...can be selected from among those described herein below...encapsulation in liposomes" (parag.0410-0411). Ni et al. further teach formulations comprising nucleic acids and biodegradable polymers such as chitosan with combinations and mixtures of other materials (page 113, parag.1032). Ni et al. further teach "formulations comprising compositions of the invention and a biodegradable polymer may also include release rate modification agents" (page 113, col.1034). Ni et al. teach that their controlled release formulations may also include release-rate modification agents and/or pore-forming agents such as fatty acids (lipids) (page 56, parags. 0537-0538). Ni et al. clearly suggests a particle comprising (1) nucleic acids, (2) the biodegradable polymer, chitosan, and (3) the release-rate modification agent, fatty acids (also known as lipids). As discussed above, Hart suggests condensing DNA with lipopolyplexes.

Claim 3 is directed to the particle of claims 1, wherein said polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 4 is directed to the particle of claim 1, wherein said polynucleotide encodes interferon gamma. Ni et al. teach interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 5 is directed to a composition comprising a particle and a pharmaceutically acceptable carrier, wherein said particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide. Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407). Hart teaches lipopolyplexes and includes teachings of compositions comprising the polymer, chitosan, suggestive of the instant claim.

Claim 6 is directed to the composition of claim 5, wherein said particle is a nanoparticle. It is well established in the art that delivery of nucleic acids in particles comprising substances such as chitosan or liposomes is in the nano-scale. Hart discloses nanosized particles of chitosan/DNA (page 203, section 3.4).

Claim 7 is directed to the composition of claim 5, wherein said polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 8 is directed to the composition of claim 5, wherein said polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 10 is directed to a method for delivery and expression of a polynucleotide within a mammal, said method comprising administering a particle to the mammal, wherein the particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide, wherein the polynucleotide is expressed in the mammal. Ni et al. teach, methods of treatment using gene therapy wherein non-replicating DNA sequences can be introduced into the cells of a mammal and provide production of the desired polypeptide for periods of up to six months," (page 124, parag.1124).

Claim 11 is directed to the method of claim 10, wherein said particle is a nanoparticle. It is well established in the art that delivery of nucleic acids in particles comprising substances such as chitosan or liposomes is in the nano-scale.

Claim 12 is directed to the method of claim 10, wherein the polynucleotide encodes a cytokine. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 13 is directed to the method of claim 10, wherein the polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272).

Claim 16 is directed to the method of claim 10, wherein the particle is administered within a composition comprising a pharmaceutically acceptable carrier. Ni et al. teach pharmaceutical compositions of the invention (page 43, parag. 0407).

Claim 17 is directed to a method for enhancing interferon-gamma expression to regulate the production of cytokines secreted by T-helper type 2 (Th2) cells, said method comprising administering an effective amount of a particle to a mammal, wherein the particle comprises chitosan, or a chitosan derivative, a lipid, and a polynucleotide encoding interferon-gamma and wherein the polynucleotide is expressed, producing interferon-gamma in the mammal. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. also teach “administration of polynucleotides…of the present invention…[modulate] proliferation, differentiation, or chemotaxis of T-cells” (page 59-60, parag.0580).

Claim 18 is directed to the method of claim 17, wherein the mammal is human. Ni et al. teach that their compositions could be used to treat humans (page 58, parag. 0563).

Claim 19 is directed to the method of claim 17, wherein the mammal is suffering from asthma. Ni et al. teach, "compositions of the invention may be used as agents for immunological disorders including…asthma." (page 7, parag.0086).

Claim 20 is directed to the method of claim 17, wherein the particle is administered to the respiratory tract of the mammal. Ni et al. teach aerosol administration of the compositions (page 58, parag. 0561).

Claim 21 is directed to a method for producing a particle comprising a complex of chitosan, or a chitosan derivative and a polynucleotide, said method comprising mixing the polynucleotide, the lipid, and the chitosan or chitosan derivative, to form the particle. Ni et al. teach formulations comprising nucleic acids and chitosan and combinations and mixtures of other materials (page 113, parag. 1032). Ni et al. teach creating the particles through a process of mixing (page 44, parag.0418).

Claim 24 is directed to the method of claim 10, wherein the particle is administered intranasally. Ni et al. teach intranasal administration (page 43, parag.0411).

Claim 25 is directed to the particle of claim 1, wherein the lipid is a cationic lipid or phospholipid. Ni et al. teach certain embodiments wherein the polynucleotide is complexed with cationic lipids (page 55, parag.0535).

Claim 26 is directed to the particle of claim 1, wherein the particle comprises chitosan. Ni et al. teaches particles comprising chitosan. Hart teaches lipopolyplexes and includes teachings of compositions comprising the polymer, chitosan, suggestive of the instant claim.

Claim 27 is directed to the particle of claim 1, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 28 is directed to the particle of claim 1, wherein said lipid is a phospholipid. Hart describes making lipoplexes that incorporate phosphatidylcholine. This would therefore be obvious to incorporate such phospholipids into the lipopolyplexes.

Claim 30 is directed to the method of claim 10, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 31 is directed to the method of claim 10 wherein the mammal is human. Ni et al. teach "therapeutic methods useful for …treating…disorder related to these novel human polypeptides" (page 1, parag.0002).

Claim 32 is directed to the method of claim 10, wherein said particle is administered to the respiratory tract of the mammal. Ni et al. teach treating lung.

Claim 33 is directed to the method of claim 17, wherein the particle is administered intranasally. Ni et al. teach intranasal delivery.

Claim 34 is directed to the method of claim 17, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 35 is directed to the method of claim 21, wherein said polynucleotide encodes interferon gamma. Ni et al. teach polynucleotides of the present invention may be useful to an agent to increase cytokine production (page 67, parag. 0666). Ni et al. teach various cytokines, including interferon gamma (page 119, parag. 1081). Ni et al. also describe recombinant DNA technology involving interferon gamma (page 26, parag. 0272). Ni et al. also teach "administration of polynucleotides…of the present invention…[modulate] proliferation, differentiation, or chemotaxis of T-cells" (page 59-60, parag.0580).

Claim 36 is directed to the method of claim 21, wherein said particle comprises a chitosan derivative. Ni et al. teach sulphated chitin derivatives. Furthermore, using a derivative of any component of a composition would be an obvious variant.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to combine the teachings of Hart and Ni et al. to produce a lipopolyplex composition of chitosan, or a chitosan derivative; a lipid; and a polynucleotide for delivery of a polynucleotide to a mammal.

The person of ordinary skill in the art would have been motivated to use chitosan in the lipopolyplexes of Hart because chitosan well known as biocompatible, non-toxic, cationic polymer used in polymer/DNA complexes. Therefore, it is an obvious substitution within the lipopolyplex composition.

An artisan would have expected success, because formulating polylipoplexes were known in the art prior to the instant application.

Therefore the compositions and methods as taught by Hart in view of Ni et al. would have been *prima facie* obvious over the compositions and methods of the instant application.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-41 recite the limitation "wherein polynucleotide-lipid inverted cylindrical micelles." The claims from which they depend do not recite this limitation. If this is a new limitation, the word, “a” is required, if it is a dependency, the word "the" is required. Otherwise, there seems to be no relationship between this phrase and the preceding claims. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 10, 21, 25, 28, 29, 31, 37-39 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (US2003/0186916, published 2 Oct 2003) in view of Vijayanathan et al. (*Biochemistry*. Dec.3, 2002, 41(48):14085-14094).

Claim 1 is directed to a nanoparticle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide. Yu et al. teach "a vector for transfecting a eukaryotic cell, comprising a nucleic acid, a nucleic acid binding polymer, a lipid-based vesicle" (page 12, claim 1 and page 3, parag.0014). Yu et al. also teach that "preferred types of nucleic acid binding polymers include polymers…[such as] chitosan" (page 3, parag.0016).

While Yu et al. do teach the constituents of instant claim 1 form a complex, Yu et al. does not explicitly teach that the complexes are nanoparticles.

However, Vijayanathan et al. teach non-viral delivery vehicles comprising polycationic lipids and cationic polymers (including chitosan) condense DNA into nanoparticles.

Claim 5 is directed to a composition comprising a nanoparticle and a pharmaceutically acceptable carrier, wherein said particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide. The compositions of Yu et al. are developed for human therapy and are therefore pharmaceutically acceptable.

Claim 10 is directed to a method for delivery and expression of a polynucleotide within a mammal, said method comprising administering a nanoparticle to the mammal, wherein the particle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide, wherein the polynucleotide is expressed in the mammal. Yu et al. describe their gene therapy compositions as expression systems appropriate for mammals.

Claim 21 is directed to a method for producing the composition of claim 1 by mixing. Yu et al. describe mixing their components.

Claim 25 is directed to the particle of claim 1, wherein said lipid is a cationic lipid. Yu et al. describe various cationic lipids.

Claim 28 is directed to the particle of claim 1, wherein said lipid is a phospholipid. Yu et al. describe various phospholipids lipids including phosphatidylcholine.

Claim 29 is directed to the particle of claim 1, wherein said polynucleotide is surrounded by a monolayer of said lipid. Yu et al. teach lipids may be arranged in monolayers or bilayers (page 6, parag. 38).

Claim 31 is directed to the method of claim 10 wherein the mammal is human. The methods of Yu et al. are used for delivery to humans.

Claims 37-39 and 41 are dependent from claims 1, 5, 10, 21 and 29 and are directed to nanoparticles which comprise polynucleotide-lipid inverted cylindrical micelles arranged in a hexagonal lattice. Vijayanathan et al. teach that non-viral delivery vehicles comprising polycationic lipids and cationic polymers (including chitosan) condense DNA into nanoparticles into columnar hexagonal liquid crystalline structures. Since the teachings of Vijayanathan et al. encompass nanoparticles comprising the same materials as Yu et al. and the instant claims, the examiner concludes the arrangement of such nanoparticles into a hexagonal lattice is a natural consequence of the chemical nature of these particles.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to combine the teachings of Yu et al. and Vijayanathan et al. to

arrive at a nanoparticle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide which form inverted cylindrical micelles arranged in a hexagonal lattice.

The person of ordinary skill in the art would have been motivated to combine these teachings because both cited references encompass particles comprising these components, but only Vijayanathan teach that the particles are nanoparticles which form inverted cylindrical micelles arranged in a hexagonal lattice, while only Yu et al. encompass embodiments of the dependent claims. Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (particles comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide; nanoparticles encompassing this general formula; and the hexagonal structure intrinsic to such particles) are taught by Yu or Vijayanathan and further they are taught in DNA delivery particles. It would be therefore predictably obvious to use a combination of these elements in a DNA-nanoparticle.

An artisan would have expected success, because both references teach condensed DNA particles.

Therefore the nanoparticles as taught by Yu et al. in view of Vijayanathan et al would have been *prima facie* obvious over the nanoparticles of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29 and 37-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002) as applied to claims 1, 5, 10, 17, and 21

above, and further in view of Vijayanathan et al. (*Biochemistry*. Dec.3, 2002, 41(48):14085-14094).

The teachings of Hart and Ni et al. are provided in the 103 rejection above.

Claims 29 and 37- 41 are dependent from claims 1, 5, 10, 17, and 21 are directed to nanoparticles which comprise polynucleotide-lipid inverted cylindrical micelles arranged in a hexagonal lattice. Vijayanathan et al. teach that non-viral delivery vehicles comprising polycationic lipids and cationic polymers (including chitosan) condense DNA into nanoparticles into columnar hexagonal liquid crystalline structures. Since the teachings of Vijayanathan et al. encompass nanoparticles comprising the same materials as Hart and Ni et al. and the instant claims, the examiner concludes the arrangement of such nanoparticles into a hexagonal lattice is a natural consequence of the chemical nature of these particles.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to combine the teachings of Hart and Ni et al and Vijayanathan et al. to arrive at a nanoparticle comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide which form inverted cylindrical micelles arranged in a hexagonal lattice.

The person of ordinary skill in the art would have been motivated to combine these teachings because both cited references encompass particles comprising these components, but only Vijayanathan teach that the particles are nanoparticles which form inverted cylindrical micelles arranged in a hexagonal lattice, while Hart and Ni et al encompass embodiments of the dependent claims. Regarding the rationale for

combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (particles comprising chitosan, or a chitosan derivative, a lipid; and a polynucleotide; nanoparticles encompassing this general formula; and the hexagonal structure intrinsic to such particles) are taught by Hart or Ni or Vijayanathan and further they are taught in DNA delivery particles. It would be therefore predictably obvious to use a combination of these elements in a DNA-nanoparticle.

An artisan would have expected success, because all the cited references teach condensed DNA particles.

Therefore the nanoparticles and methods as taught by Hart in view of Ni et al. and further in view of Vijayanathan et al would have been *prima facie* obvious over the nanoparticles and methods of the instant application.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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